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FACT SHEET

joseph disease

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What is Joseph disease?

Joseph disease is a fatal genetic disorder of the nervous system that cripples and paralyzes while leaving the intellect intact. The disease is characterized by weakness in the arms and legs and a general loss of motor control that eventually confines the patient to a wheelchair. Symptoms appear when a defective gene causes a breakdown and loss of cells in specific areas of the brain known as the striatum, the cerebellum, and the substantia nigra, but what sets this process in motion is still unknown. There is as yet no effective treatment.

Joseph disease, first documented in the 1970's, is named for Antone Joseph, a Portuguese sailor with the defective gene who came to California in 1845. The disease occurs primarily in people of Portuguese ancestry, but it has also been found in other ethnic groups, nationalities, and races.

What are its symptoms?

Some symptoms of Joseph disease resemble those of other neurological disorders such as multiple sclerosis and Parkinson's disease. A careful diagnosis is therefore important and should be made by a physician with expertise in neurology. Symptoms of Joseph disease include

- weakness in the arms and legs
- spasticity, especially in the legs
- awkward body movements
- staggering, lurching gait—easily mistaken for drunkenness
- difficulty with speech and swallowing
- involuntary eye movements
- double vision
- bulging appearance of the eyes
- frequent urination.

Symptoms most commonly begin between the ages of 15 and 35, but may appear a little earlier or much later in life. Progression may be fast or slow, and life expectancy ranges from 10 to 30 years after the disease begins.

How Is Joseph disease inherited?

Joseph disease is an autosomal dominant disorder. This means that each child of an affected parent has a 50 percent chance of inheriting the defective gene. Joseph disease does not skip generations, but people at risk who escape the disease will not pass it on to their children or future generations. However, since there is no test yet to identify carriers of the defective gene, and since symptoms sometimes do not appear until later in life, people at risk must decide whether to have children without knowing for sure whether they might pass the gene on. As with any inherited disorder, Joseph disease is not contagious and cannot be "caught" by people who are not at risk.

How is the disease diagnosed?

Joseph disease is diagnosed by identifying the typical symptoms in a family in which the disease occurs. Characteristic features include progressive difficulty in walking and speech beginning in the late teen years or in the 20's through the 50's. The gait is abnormal due to spasticity and speech is slurred because of spastic weakness in the throat muscles. The Joseph disease patient may be unable to look upward or inward, and the eyes may oscillate from side to side.

Late-onset Joseph disease, the type that begins when a patient is 70 or older, is characterized by an uncoordinated gait that may cause the patient to stumble or fall, the slurring speech, and the loss of muscle in the arms and legs.

Neurologists have classified Joseph disease into three types, depending on age at onset and characteristic symptoms. But it is uncertain whether the three types are subtypes of the same disease or three separate diseases. Because the three types have at times borne different names, the plural term *Joseph diseases* has been used.

What research is being done?

The National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) conducts and supports research on all disorders of the nervous system, including Joseph disease. Much of this research is relevant to different aspects of Joseph disease, and may lead to treatment, a cure, and eventually prevention.

NINCDS is studying normal and defective genes to understand how inherited characteristics are transmitted. With such knowledge and improved genetic engineering techniques, intervention and a cure for inherited disorders like Joseph disease might be possible.

One thrust of Joseph disease research is to find a "genetic marker" which could be used to identify carriers of the defective gene before they have children. NINCDS-supported scientists developed techniques that allowed them to find one such marker for Huntington's disease. They are now using this knowledge and looking for additional markers so that a presymptomatic test can be developed for people at risk for Huntington's. Investigators hope that the new genetic methodology used in this work can be applied to the development of a test for Joseph disease.

A number of other neurological disorders share symptoms with Joseph disease, and research conducted on these disorders should benefit Joseph disease patients. NINCDS scientists are studying the degeneration of the brain's cerebellum that occurs in the ataxias. This type of degeneration produces the kind of spasticity and tremor seen in Joseph disease. NINCDS research on motor neuron diseases, including amyotrophic lateral sclerosis and spastic paraplegia, focuses on the deterioration of certain nerve cells in the spinal cord that also degenerate in Joseph disease.

Much NINCDS-supported research on Parkinson's disease is relevant to Joseph disease. The brain's substantia nigra area is under study

because it deteriorates in both disorders. The development of drugs that will increase dopamine—a brain chemical missing in Parkinson's disease—may produce an effective therapy for symptoms of Joseph disease. Investigators using a special imaging technique called positron emission tomography (PET) have already produced the first pictures of dopamine at work in the living brain. Further studies with PET may increase our understanding of dopamine's possible connection to Joseph disease.

Some scientists are studying the role of enzymes in olivopontocerebellar atrophy, a rare inherited neurological disorder similar to Joseph disease. These studies may uncover an enzyme defect that could also be responsible for Joseph disease.

Some patients with Joseph disease have high blood glucose levels and abnormal glucose tolerance test results. Research has also shown that some patients have reduced levels of homovanillic acid (a nervous system chemical) in their spinal fluid. These abnormalities are of special interest to scientists studying Joseph disease.

How can I help research?

The National Institute of Neurological and Communicative Disorders and Stroke and the National Institute of Mental Health support two national human brain specimen banks, one at the Wadsworth Veterans Administration Hospital in Los Angeles and the other at McLean Hospital near Boston. These banks supply investigators around the world with tissue from patients with neurological and psychiatric diseases. Both banks need brain tissue from Joseph disease patients to enable scientists to study this disorder more intensely. Prospective donors should write to:

Dr. Wallace W. Tourtellotte, Director
Human Neurospecimen Bank
VA Wadsworth Medical Center
Building 212, Room 31
Los Angeles, California 90073
Telephone: (213) 824-4307 (Call collect.)

Dr. Edward D. Bird, Director
Brain Tissue Bank, Maliman Research Center
McLean Hospital
115 Mill Street
Belmont, Massachusetts 02178
Telephone: (617) 855-2400 (Call collect 24 hours a day.)

Where can I get help?

The International Joseph Diseases Foundation is a voluntary, nonprofit organization of concerned people including patients, their families and friends, and health-care professionals. The foundation provides information about the disease, supports and conducts clinical research, and helps patients find medical, social, and genetic counseling services.
Contact:

International Joseph Diseases Foundation, Inc.
P.O. Box 2550
Livermore, California 94550
Telephone: (415) 455-0706

NINCDS information

For additional information concerning Joseph disease research supported by the National Institute of Neurological and Communicative Disorders and Stroke, contact:

Office of Scientific and Health Reports
National Institute of Neurological and
Communicative Disorders and Stroke
Building 31, Room 8A-06
National Institutes of Health
Bethesda, Maryland 20892
(301) 496-5751

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Office of Scientific and Health Reports
National Institute of Neurological and
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Bethesda, Maryland 20892

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